Fluid management in hemorrhagic shock

Andreas Markl-Le-Levé, Ingrid Haller and Mirjam Bachler

Downloaded from http://journals.lww.com/co-anesthesiology by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 04/24/2025

Purpose of review
Fluid management in hemorrhagic shock is a controversial topic, and there are evolving clinical guidelines and evidence-based practice. This review aims to highlight the physiological aspects in the light of current evidence on which volume replacement solution to use.

Recent findings
Current evidence and international guidelines are shifting from a liberal to a restrictive fluid resuscitation strategy, emphasizing the potential risks associated with aggressive fluid therapy. The 'lethal triad of trauma' (hypoperfusion, acidosis, and coagulopathy) plays a crucial role in the pathophysiology of hemorrhagic shock. While crystalloids are less effective at restoring intravascular volume, colloids (especially hydroxyethyl starch) have raised concerns about potential adverse effects on renal function and coagulation. Albumin remains controversial, as studies showing no clear benefit and an increased mortality in traumatic brain injury patients. Fresh frozen plasma, may be useful in massive transfusion situations but is not recommended for volume resuscitation.

Summary
The management of fluid resuscitation evolves, with a trend toward more restrictive strategies. Crystalloids, although less effective for severe volume depletion, remain a cornerstone of initial resuscitation. Among the colloids, gelatin-based solutions and albumin can be used when crystalloids are inadequate, while hydroxyethyl starch is no longer recommended.

Keywords
colloid, crystalloid, hemorrhage, trauma, volume replacement

INTRODUCTION

The debate about the optimal approach to volume replacement in hemorrhagic shock indeed highlights the gap between evolving clinical guidelines and robust evidence-based support. The shift from Advanced Trauma Life Support 1997s recommendation of 8 L of combined crystalloid and colloid fluids to the 2019 focus on limiting crystalloid infusion to just 1 L underscores a trend toward more restrictive fluid resuscitation [1]. This evolution reflects growing awareness of the potential harms of aggressive fluid therapy, such as dilutional coagulopathy and increased interstitial edema, but it remains largely based on expert opinion and retrospective analyses rather than high-quality randomized controlled trials.

The current European Trauma Guidelines from 2023 endorsement for permissive hypotension is similarly based on limited evidence [2▪]. The fact that Bickel *et al.*'s [3] study from 1994, often cited in support of permissive hypotension, is acknowledged to have methodological limitations, including its limited population and the challenges of extrapolating findings to broader clinical scenarios. Nevertheless, permissive hypotension has gained traction, particularly in the prehospital and early inhospital setting, where controlling bleeding and minimizing the risk of clot dislodgement take precedence over resuscitation from hypovolemic shock.

The decline in the use of synthetic colloids following the European Medicines Agency's Pharmacovigilance Risk Assessment Committee's (PRAC) 2018 recommendations reflects safety concerns, including the risk of renal injury and coagulopathy, rather than definitive evidence of superior alternatives [4]. While balanced crystalloids and blood products (e.g. plasma, platelets, and red blood cells) are increasingly favored, the lack of definitive evidence comparing these strategies continues to leave clinicians navigating a complex and uncertain landscape.

Department of Anesthesiology and Intensive Care Medicine, Trauma Intensive Care Unit, Medical University of Innsbruck, Innsbruck, Austria

Correspondence to Andreas Markl-Le-Lev´e, MD, Department of Anesthesiology and Intensive Care Medicine, Trauma Intensive Care Unit, Medical University of Innsbruck, Anichstrasse 35, A-6020 Innsbruck, Austria
E-mail: andreas.markl-le-leve@tirol-kliniken.at

Curr Opin Anesthesiol XXX, XXX:XXXX–XXXX
DOI:10.1097/ACO.0000000000001481

0952-7907 Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2025 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

SHOUT
SHARE
IT

Downloaded from http://journals.lww.com/co-anesthesiology by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 04/24/2025

KEY POINTS

- The 'lethal triad of trauma' (hypoperfusion, acidosis, and coagulopathy) plays a critical role in the pathophysiology of hemorrhagic shock, with recent evidence highlighting the central role of hypoperfusion and endotheliopathy in driving trauma-induced coagulopathy.
- Current guidelines emphasize the potential risks of aggressive fluid therapy, including dilutional coagulopathy and increased interstitial edema, and shift toward restrictive fluid resuscitation strategies in hemorrhagic shock.
- Gelatin-based solutions and albumin can be used when crystalloids are inadequate for resuscitation; however, hydroxyethyl starch is no longer recommended due to concerns about adverse effects.

Ultimately, the debate underscores the urgent need for well-designed clinical trials examining the timing, type, and volume of fluids in hemorrhagic shock. Until then, clinical decisions will likely continue to be influenced by institutional protocols, emerging trends, and individual patient factors, rather than a unified evidence-based standard.

THE LETHAL TRIAD OF DEATH – SHOCK – ACIDOSIS AND COAGULOPATHY

The 'lethal triad of trauma', consisting of hypoperfusion, acidosis, and coagulopathy, is a hallmark of severe trauma and reflects a self-perpetuating cycle of physiologic dysfunction. Recent evidence, particularly that of Moore *et al*. [5], has highlighted the central role of hypoperfusion and endotheliopathy in driving trauma-induced coagulopathy (TIC).

Shock-related coagulopathy in trauma results from a complex interplay of hypoperfusion, acidosis, endothelial dysfunction, fibrinolytic dysregulation, and clotting factor depletion due to hemorrhage. Activation of the protein C pathway, fibrinogen consumption and hyperfibrinolysis, and impaired thrombin generation further exacerbate the inability to form stable clots. Systemic inflammation, induced by endotheliopathy, aggravates this coagulopathy by causing platelet dysfunction and excessive clotting factor consumption [5]. These complex relationships between hypoperfusion, endotheliopathy, and coagulopathy underscore the challenges and needs in managing hemorrhagic shock. While restrictive fluid resuscitation aims to prevent dilutional coagulopathy, this approach may be too simplistic to address the multifactorial pathophysiology of TIC. A deeper understanding of these mechanisms is essential to the development of more nuanced and effective therapeutic strategies to achieve normovolemia in hemorrhagic shock without inducing deleterious adverse side effects.

CRYSTALLOIDS OR COLLOIDS?

The debate as to whether colloids are generally superior to crystalloids in hemorrhagic shock remains unresolved. Current guidelines and recommendations for the use of colloids in hemorrhagic shock are influenced by the PRAC recommendation, based on the results of the VISEP [6] and 6S [7] trials in septic but not hemorrhagic shock. However, Annane *et al*. [8] found conflicting results even also in patients with septic shock. Within the CRISTAL trial, patients who received colloids showed an improved 90-day survival [8]. However, extrapolating results from septic shock trials, where HES was associated with renal failure, to hemorrhagic shock is not considered appropriate. Specifically, with regard to renal failure, positive results have been observed with HES even in hemorrhagic shock, as demonstrated by the FIRST study [9]. In this study, HES, unlike crystalloid fluids, was able to prevent from prerenal failure in trauma-associated hemorrhagic shock. In addition, lactate clearance, a marker of effective volume replacement, was improved compared with crystalloids in this study [9].

Crystalloids are less effective at restoring intravascular volume due to their tendency to diffuse into the interstitial space, which can cause edema. The intravascular volume effect of crystalloids is at least 18% for 20 min, whereas synthetic or natural colloids have a volume effect of up to 100% for up to several hours [10] (Fig. 1). A meta-analysis by Martin and Basset [11], that included 55 studies with 27 036 patients, concluded that crystalloids were less effective than colloids in stabilizing resuscitation endpoints.

Dilutional coagulopathy is a consequence of fluid resuscitation, with the degree of coagulopathy

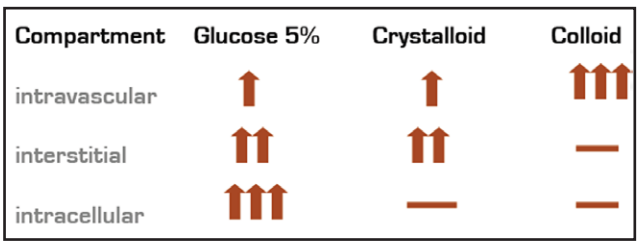

FIGURE 1. Volume effect of different solutions.

Copyright © 2025 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

Downloaded from http://journals.lww.com/co-anesthesiology by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 04/24/2025

being related to the amount and type of fluid administered. The primary problem that triggers dilutional coagulopathy is impaired fibrin polymerization. Among the various fluids, hydroxyethyl starch (HES) has been shown to have the most pronounced negative effect on coagulation [12].

These adverse effects of intravascular volume therapy can be mitigated by increasing fibrinogen concentrations. Administration of fibrinogen concentrate, even during ongoing blood loss and continued intravascular volume replacement, has been shown to reverse these coagulopathic effects [12]. This approach helps restore normal fibrinogen levels, which are critical for proper clot formation and to counteract the effects of fluid-induced dilutional coagulopathy.

BALANCED VERSUS UNBALANCED FLUIDS

The choice of fluid resuscitation should also consider its impact on acid-base balance. Unbalanced, saline-based fluids are associated with hyperchloremic acidosis, which may exacerbate tissue hypoperfusion and organ dysfunction. Although the clinical significance of hyperchloremic acidosis remains controversial, balanced solutions are generally preferred. The British Consensus Guideline on Intravenous Fluid Therapy for Adult Surgical Patients recommends balanced solutions over saline for volume replacement [13]. A study in elderly surgical patients demonstrated that balanced crystalloids combined with colloids prevented metabolic acidosis and improved gastric mucosal perfusion compared with saline-based solutions [14].

SYNTHETIC COLLOIDS

Gelatin solutions

The use of gelatin in massive transfusion protocols dates back to the Korean War in 1950 [15]. However, since that time the formulation has undergone several significant changes and improvements from oxypolygelatin (1951) to urea-cross linked gelatin (1958), succinylated gelatin (1962), and succinylated gelatin dissolved in balanced solutions (2013). Gelatins have been used for over 100 years, and there are some doubts about their effects on renal function, without much clinical evidence at the moment [16,17]. From a pharmacokinetic perspective, gelatin molecules are cleaved into smaller fragments by nonspecific peptidases in plasma, which are subsequently metabolized and eliminated by renal enzyme systems once they fall below the renal threshold. This process results in a faster rate of metabolism and elimination rate compared with other artificial colloids, such as HES.

According to current knowledge, gelatin and its derivatives are not stored in tissues or organs, thus eliminating the risk of storage-related complications. There is no maximum daily dose for gelatin solutions. This allows gelatin solutions to be infused at higher doses, maintaining cardiac preload and may reduce the risk of prerenal renal failure [18].

Reports of a higher incidence of anaphylaxis with gelatin-based colloids often refer to Haemaccel. Haemaccel, urea-linked gelatin, has a relatively higher risk of anaphylaxis of 0.08–0.3% compared with Gelofusine, which has a significantly lower risk, estimated at 0.035–0.06% due to its succinylated gelatin formulation, which has a lower immunogenic potential [19]. However, Haemaccel is not anymore available in the market.

The volume effect of succinylated gelatin is comparable to that of HES or albumin and superior to that of crystalloids (Fig. 2). In contrast, the urea-linked Haemaccel, being a globular molecule, has a lower volume effect. Succinylated gelatin, on the other hand, has an elongated molecular structure with numerous negative charges, which enhances its intravascular persistence and contributes to its improved volume-expanding properties.

In addition to dilution, gelatin-based solutions have specific effects on the coagulation system. Primarily, they interfere with fibrin polymerization and disrupt the cross-linking of fibrin monomers. In addition, decreased clot elasticity and decreased clot weight have been observed after gelatin administration. Jonge *et al.* [20] compared the anticoagulant effects of a 1000 ml gelatin infusion to those of a 1000 ml infusion of 0.9% NaCl solution in healthy volunteers. Reductions in thrombin generation (as

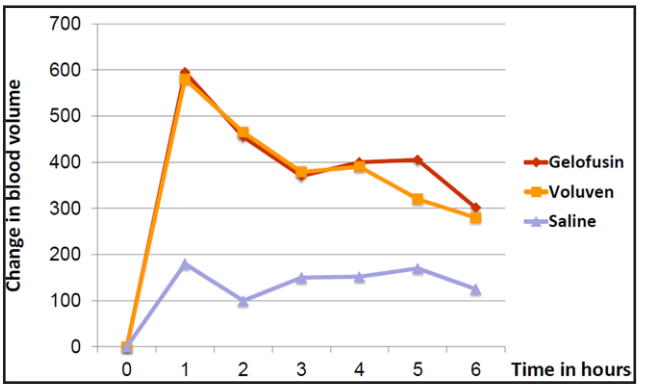

FIGURE 2. Volume effect of 1 L of saline, 6% HES 130/0.4, and succinylated gelatin (Lobo *et al.* [10]). HES, hydroxyethyl starch.

Copyright © 2025 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

measured by thrombin-antithrombin complexes), von Willebrand factor levels, and ristocetin-induced platelet aggregation were observed in the gelatin group compared with the NaCl-treated group [20].

Although gelatin is classified as a synthetic colloid and is typically associated with a number of negative outcomes, particularly regarding renal function, the GENIUS study [21] (currently under publication) demonstrated no side effects on renal function with gelatin in patients with septic shock.

Advantages of succinylated gelatin include the following:

1. Improved volume effect compared with crystalloids.
2. Reduced effects on coagulation and fibrin polymerization compared with HES.
3. Lack of accumulation in the reticuloendothelial system (RES) or other tissues.
4. No clinically relevant effect on renal function.

Disadvantages of succinylated gelatin include the following:

1. Impaired fibrin polymerization and alteration of the structure of fibrin networks, compared with crystalloids.
2. Potential risk of causing severe anaphylactic reactions.

Hydroxyethyl starch

HES have long been used as plasma volume expanders in the treatment of hemorrhagic shock, providing a rapid and effective means of restoring intravascular volume. Their colloidal properties allow for significant and sustained plasma volume expansion compared with crystalloids, which are rapidly redistributed into the interstitial space. However, the use of HES has raised concerns about potential adverse effects on renal function, coagulation, and mortality [6,7], particularly in septic shock, which has led to ongoing debate and investigation.

Several clinical studies have proven the association between the administration of HES and acute kidney injury (AKI) particularly in septic shock [6,7,22,23]. This risk appears to be dose-dependent and is influenced by the molecular weight and degree of substitution of the starch. High-molecular-weight HES preparations, particularly those with a high degree of substitution, have shown a greater tendency to impair renal function. Nevertheless, in the FIRST trial [9], hypovolemia-induced prerenal renal failure in hemorrhagic shock was prevented and the negative renal effects were overcome by restoring hypovolemic shock with the administration of HES compared with saline.

HES also affects coagulation beyond dilutional coagulopathy by interfering with fibrin polymerization and platelet function [24,25], further complicating its role in the resuscitation of trauma patients with hemorrhagic shock. The effects on fibrin polymerization are significantly more pronounced with HES than with gelatin. These coagulation impairments may exacerbate bleeding tendencies, a critical concern in trauma care where coagulopathy is already prevalent.

Early clinical trials comparing HES to saline showed mixed results. While HES provided superior volume expansion and hemodynamic stabilization in the short term, saline was less likely to induce renal dysfunction and coagulopathy. Subsequent large-scale studies and meta-analyses have largely favored saline or balanced crystalloids over HES due to a lower risk profile.

Advantages of HES include the following:

1. Improved volume effect compared with crystalloids.

Disadvantages of HES include the following:

1. Increased impairment of coagulation especially fibrin polymerization and alteration of the structure of fibrin networks, compared with crystalloids and gelatin.
2. Accumulation in the RES or other tissues.
3. Increased effects on coagulation and especially on fibrin polymerization compared with gelatin or crystalloids.
4. Impairment of the renal function.

NATURAL COLLOIDS

Albumin

Albumin has a limited and controversial role in the management of trauma-induced shock. As a natural colloid, albumin is responsible for maintaining colloid osmotic pressure and binds to several molecules in the blood. However, its clinical application in trauma is overshadowed by significant physiological limitations, safety concerns, and cost issues.

One of the most important findings regarding albumin in trauma care comes from its effects on patients with traumatic brain injury (TBI). In the SAFE study [26], a subgroup analysis showed an increased mortality rate in TBI patients treated with albumin compared with crystalloids. This prompted further research, culminating in the SAFE-TBI study [27], which confirmed these findings. The underlying mechanism

Copyright © 2025 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

Downloaded from http://journals.lww.com/co-anesthesiology by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 04/24/2025

Downloaded from http://journals.lww.com/co-anesthesiology by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 04/24/2025

is thought to be related to the hypoosmolar property of 4% albumin solutions, which can lead to increased cerebral edema and increased intracranial pressure. These findings have led to the use of albumin in patients with TBI being strongly discouraged.

Outside of TBI, albumin has not shown a clear benefit in trauma patients overall. While albumin may reduce the need for vasopressors and in some cases provide a modest improvement in hemodynamic stability, these benefits have not translated into reduced mortality. The SAFE trial [26], which evaluated albumin versus normal saline in critically ill patients rather than trauma patients, showed no significant difference in 28-day mortality in general ICU patients. This lack of survival benefit combined with the high cost of albumin has further limited its role in trauma resuscitation.

Another critical limitation of albumin in trauma therapy is its potential to exacerbate coagulopathy, which is common to all colloids. Trauma patients are often already at risk for coagulopathy due to massive bleeding, hypothermia, and acidosis. Albumin, like other colloids, dilutes coagulation factors when administered in large amounts and can exacerbate this condition.

The cost of albumin is another major barrier to its widespread use in volume resuscitation [28,29]. Albumin is significantly more expensive than crystalloids and synthetic colloids, yet there is no consistent evidence of superior outcomes. This economic consideration is particularly important in resource-constrained settings where the availability of expensive therapies is limited.

Given these factors, albumin is generally not recommended as a first-line fluid for resuscitation of trauma patients. Albumin may occasionally be considered in very specific cases where its oncotic properties are considered beneficial, but these cases are rare in trauma care. For the vast majority of trauma patients, the risks and costs associated with albumin may outweigh the potential benefits.

Advantages of albumin include the following:

1. Improved volume effect compared with crystalloids.
2. No clinically relevant impact on renal function compared with HES.

Disadvantages of albumin include the following:

1. Increased coagulopathy compared with crystalloids.
2. Worse outcome in patients with TBI.
3. Potential risk of causing severe anaphylactic reactions.
4. High cost and limited availability.

FRESH FROZEN PLASMA

Although not recommended for volume resuscitation in trauma [2▪▪] or sepsis [30,31▪], plasma may be useful in clinical scenarios where it is required not only to expand blood volume but also to meet other needs, such as correction of coagulopathies or replacement of certain blood proteins. Fresh frozen plasma (FFP), either single donor, pooled or freeze-dried plasma (FDP), is the most commonly used type of plasma.

In severe trauma or major surgery where there is massive blood loss and packed red blood cells are administered, plasma is also often administered to maintain the balance of red blood cells and clotting factors to prevent dilutional coagulopathy. However, the European Guideline on the management of major bleeding and coagulopathy after trauma advises against the use of plasma in patients without major bleeding because of its potential side effects and cost. FFP or high fibrinogen concentrate/cryoprecipitate is recommended for initial coagulation resuscitation of patients with massive bleeding or those expected to bleed, but FFP should not be used to correct hypofibrinogenemia, which is the main and first missing factor in TIC [2▪▪].

Due to conflicting evidence, the European Trauma Guidelines neither support nor oppose the use of plasma in the prehospital setting [2▪▪]. The main evidence for the use of plasma in the prehospital phase comes from two pragmatic randomized controlled trials, PAMPer [32] and COMBAT [33], which provided conflicting results. A reduction in mortality was seen only at 24 h, whereas survival was unchanged at 1 month. In contrast, a meta-analysis has emphasized the long-term reduction in mortality achieved by prehospital use of erythrocytes and plasma, although mortality remained unchanged at 24 h. Other studies have found no significant reduction in mortality or the incidence of multiorgan failure [34▪]. Thus, the effect of plasma transfusion on mortality and multiorgan failure cannot be clearly demonstrated. It is important to note that the studies supporting the use of plasma are primarily from the USA, where trauma mortality is significantly higher according to the Injury Severity Score compared with Central Europe [35].

Recent publications advocate FDP as an attractive alternative for prehospital hemorrhage management, highlighting its logistical advantages and potential in trauma care, especially in military contexts [36]. Lyophilized cryoprecipitate and FDP have shown efficacy in reducing trauma-induced endotheliopathy and providing organ protection similar to FFP [37]. Nevertheless, these experimental and/or laboratory-guided results could not be confirmed in clinical practice. The adverse

0952-7907 Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2025 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

effects of plasma transfusion, such as transfusion-associated circulatory overload and transfusion-related acute lung injury, should not be overlooked. A study by Nienaber *et al*. [38] found that FFP therapy alone was associated with a higher rate of multiple organ failure than with therapy with factor concentrates alone. Similarly, the high-profile RETIC trial [39] showed numerically higher rates of multiple organ failure in patients treated with plasma compared with those receiving coagulation factor concentrates alone and was terminated early for safety reasons. In addition, plasma transfusion is also associated with increased morbidity and mortality, particularly in critically ill patients [31▪,40–42].

Therefore, coagulation factor concentrates may provide a more accurate, efficient, and safer alternative to plasma for the treatment of bleeding in trauma patients. This targeted approach to coagulation management, coupled with logistical and safety advantages, makes factor concentrates an increasingly preferred option in emergency and trauma care.

CONCLUSION

Crystalloids are not very effective for volume replacement after major blood loss or in cases of severe intravascular volume depletion. The administration of large amounts of crystalloids can lead to edema, which may impair microcirculation. While there is no strong evidence that balanced solutions improve mortality or morbidity outcomes, their use prevents acidosis and maintains metabolic stability better than saline. Current recommendations suggest that gelatin-based solutions and albumin can be used interchangeably for hypovolemia when the effect of crystalloids is inadequate. In addition, HES is no longer recommended due to its significantly higher spectrum of side effects compared with albumin and gelatin [42]. The debate about which volume replacement solution is best for specific indications will continue, and further studies are needed to clarify this issue.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

A.M.-L.L. received travel expenses from Pfizer and Menarini. M.B. received study grants and lecture fees from CSL, Octapharm, and Mitsubishi Pharma. For I.H., there are no conflicts of interest.

REFERENCES

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

1. Galvagno SM, Jr, Nahmias JT, Young DA. Advanced Trauma Life Support(®) Update 2019: management and applications for adults and special populations. Anesthesiol Clin 2019; 37:13–32.
2. ▪▪ Rossaint R, Afshari A, Bouillon B, *et al*. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. Crit Care 2023; 27:80.

By offering evidence-based, comprehensive, and up-to-date recommendations on fluid resuscitation and coagulopathy management in trauma, this work serves as an invaluable resource for clinicians and researchers in the field.

3. Bickell WH, Wall MJ, Jr, Pepe PE, *et al*. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. N Engl J Med 1994; 331:1105–1109.
4. Annane D, Fuchs-Buder T, Zoellner C, *et al*. EMA recommendation to suspend HES is hazardous. Lancet 2018; 391:736–738.
5. Moore EE, Moore HB, Kornblith LZ, *et al*. Trauma-induced coagulopathy. Nat Rev Dis Primers 2021; 7:30.
6. Brunkhorst FM, Engel C, Bloos F, *et al*; German Competence Network Sepsis (SepNet). Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med 2008; 358:125–139.
7. Perner A, Haase N, Guttormsen AB, *et al*; 6S Trial Group. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. N Engl J Med 2012; 367:124–134.
8. Annane D, Siami S, Jaber S, *et al*; CRISTAL Investigators. Effects of fluid resuscitation with colloids vs crystalloids on mortality in critically ill patients presenting with hypovolemic shock: the CRISTAL randomized trial. JAMA 2013; 310:1809–1817.
9. James MF, Michell WL, Joubert IA, *et al*. Resuscitation with hydroxyethyl starch improves renal function and lactate clearance in penetrating trauma in a randomized controlled study: the FIRST trial (Fluids in Resuscitation of Severe Trauma). Br J Anaesth 2011; 107:693–702.
10. Lobo DN, Stanga Z, Aloysius MM, *et al*. Effect of volume loading with 1 liter intravenous infusions of 0.9% saline, 4% succinylated gelatine (Gelofusine) and 6% hydroxyethyl starch (Voluven) on blood volume and endocrine responses: a randomized, three-way crossover study in healthy volunteers. Crit Care Med 2010; 38:464–470.
11. Martin GS, Bassett P. Crystalloids vs. colloids for fluid resuscitation in the intensive care unit: a systematic review and meta-analysis. J Crit Care 2019; 50:144–154.
12. Mittermayr M, Streif W, Haas T, *et al*. Hemostatic changes after crystalloid or colloid fluid administration during major orthopedic surgery: the role of fibrinogen administration. Anesth Analg 2007; 105:905–917, table of contents.
13. Powell-Tuck J, Allison SP, Gosling P, *et al*. Summary of the British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients (GIFTASUP) – for comment. J Intensive Care Soc 2009; 10:13–15.
14. Wilkes NJ, Woolf R, Mutch M, *et al*. The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid-base and electrolyte status and gastric mucosal perfusion in elderly surgical patients. Anesth Analg 2001; 93:811–816.
15. Pearce FJ, Lyons WS. Logistics of parenteral fluids in battlefield resuscitation. Mil Med 1999; 164:653–655.
16. Koponen T, Musialowicz T, Lahtinen P. Gelatin and the risk of acute kidney injury after cardiac surgery. Acta Anaesthesiol Scand 2022; 66:215–222.
17. Thomas-Rueddel DO, Vlasakov V, Reinhart K, *et al*. Safety of gelatin for volume resuscitation – a systematic review and meta-analysis. Intensive Care Med 2012; 38:1134–1142.
18. Thiel H, *et al*. Fluid and volume replacement. In: Thiel H, *et al*., editors. Anesthesiological pharmacotherapy: pharmacology: perioperative pharmacotherapy. Stuttgart: Thieme; 2014. http://www.thieme-connect.de/products/ebooks/lookinside/10.1055/b-0034-94904.
19. Russell WJ, Fenwick DG. Anaphylaxis to Haemaccel and cross reactivity to Gelofusin. Anaesth Intensive Care 2002; 30:481–483.
20. Jonge E de, Levi M, Berends F, *et al*. Impaired haemostasis by intravenous administration of a gelatin-based plasma expander in human subjects. Thromb Haemost 1998; 79:286–290.
21. Marx G, Zacharowski K, Ichai C, *et al*. Efficacy and safety of early target-controlled plasma volume replacement with a balanced gelatine solution versus a balanced electrolyte solution in patients with severe sepsis/septic shock: study protocol, design, and rationale of a prospective, randomized, controlled, double-blind, multicentric, international clinical trial: GENIUS-Gelatine use in ICU and sepsis. Trials 2021; 22:376.

Copyright © 2025 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

Downloaded from http://journals.lww.com/co-anesthesiology by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 04/24/2025

22. Zampieri FG, Bagshaw SM, Semler MW. Fluid therapy for critically Ill adults with sepsis: a review. JAMA 2023; 329:1967–1980.

23. Rochwerg B, Alhazzani W, Gibson A, *et al*; FISSH Group (Fluids in Sepsis and Septic Shock). Fluid type and the use of renal replacement therapy in sepsis: a systematic review and network meta-analysis. Intensive Care Med 2015; 41:1561–1571.

24. Kam P, Varanasi S, Yang KX. The effects of haemodilution with succinylated gelatin solution on coagulation in vitro as assessed by thromboelastometry and impedance (multiple electrode) aggregometry. Anaesth Intensive Care 2018; 46:272–277.

25. Palmaers T, Krämer E, Hinsenkamp J, *et al*. Mannitol and the combination of mannitol and gelatin impair whole blood coagulation and the platelet function in vitro. Turk J Anaesthesiol Reanim 2019; 47:199–205.

26. Finfer S, Bellomo R, Boyce N, *et al*; SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004; 350:2247–2256.

27. Myburgh J, Cooper DJ, Finfer S, *et al*; SAFE Study Investigators. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. N Engl J Med 2007; 357:874–884.

28. Dingankar AR, Cave DA, Anand V, *et al*. Albumin 5% versus crystalloids for fluid resuscitation in children after cardiac surgery. Pediatr Crit Care Med 2018; 19:846–853.

29. Jiang L, Jiang S, Zhang M, *et al*. Albumin versus other fluids for fluid resuscitation in patients with sepsis: a meta-analysis. PLoS One 2014; 9:e114666.

30. Evans L, Rhodes A, Alhazzani W, *et al*. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med 2021; 49:e1063–e1143.

31. ▪ Wang R, Liu R, Xu Z. Association between plasma transfusion and in-hospital mortality in critically ill patients with sepsis-induced coagulopathy. Shock 2023; 60:545–552.

This study investigates the association between plasma transfusion and inhospital mortality in critically ill patients with sepsis-induced coagulopathy. Importantly, the study found that increased plasma transfusion was associated with increased mortality in a dose-dependent manner, highlighting the need for judicious use of plasma and careful consideration of risks versus benefits when making plasma transfusion decisions.

32. Sperry JL, Guyette FX, Brown JB, *et al*; PAMPer Study Group. Prehospital plasma during air medical transport in trauma patients at risk for hemorrhagic shock. N Engl J Med 2018; 379:315–326.

33. Moore HB, Moore EE, Chapman MP, *et al*. Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial. Lancet 2018; 392:283–291.

34. ▪ Abuelazm M, Rezq H, Mahmoud A, *et al*. The efficacy and safety of pre-hospital plasma in patients at risk for hemorrhagic shock: an updated systematic review and meta-analysis of randomized controlled trials. Eur J Trauma Emerg Surg 2024; 50:2697–2707.

This paper provides a good summary of some recent randomized controlled trials (RCTs) in the field of fluid resuscitation with plasma and its missing impact on improved survival in trauma patients.

35. Fenger-Eriksen C, Fries D, David JS, *et al*. Pre-hospital plasma transfusion: a valuable coagulation support or an expensive fluid therapy? Crit Care 2019; 23:238.

36. Polk TM, Gurney JM, Riggs LE, *et al*. Dried plasma: an urgent priority for trauma readiness. J Trauma Acute Care Surg 2023; 95:S4–S6.

37. Zeineddin A, Wu F, Dong JF, *et al*. Early lyophilized cryoprecipitate enhances the ADAMTS13/VWF ratio to reduce systemic endotheliopathy and lessen lung injury in a mouse multiple-trauma hemorrhage model. J Trauma Acute Care Surg 2023; 95:S137–S143.

38. Nienaber U, Innerhofer P, Westermann I, *et al*. The impact of fresh frozen plasma vs coagulation factor concentrates on morbidity and mortality in trauma-associated haemorrhage and massive transfusion. Injury 2011; 42:697–701.

39. Innerhofer P, Fries D, Mittermayr M, *et al*. Reversal of trauma-induced coagulopathy using first-line coagulation factor concentrates or fresh frozen plasma (RETIC): a single-centre, parallel-group, open-label, randomised trial. Lancet Haematol 2017; 4:e258–e271.

40. Neto AS, Juffermans NP, Hemmes SNT, *et al*. Interaction between perioperative blood transfusion, tidal volume, airway pressure and postoperative ARDS: an individual patient data meta-analysis. Ann Transl Med 2018; 6:23.

41. Sarani B, Dunkman WJ, Dean L, *et al*. Transfusion of fresh frozen plasma in critically ill surgical patients is associated with an increased risk of infection. Crit Care Med 2008; 36:1114–1118.

42. Xu X, Zhang Y, Tang B, *et al*. Association between perioperative plasma transfusion and in-hospital mortality in patients undergoing surgeries without massive transfusion: a nationwide retrospective cohort study. Front Med (Lausanne) 2023; 10:1130359.

Downloaded from http://journals.lww.com/co-anesthesiology by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 04/24/2025

0952-7907 Copyright © 2025 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2025 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.